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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,358	06/26/2003	Eduardo M. Lasalvia-Prisco	1.241.03	6124

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EXAMINER	
SANG, HONG	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/607,358	LASALVIA-PRISCO, EDUARDO M.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *1-59,66 and 68-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-65 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Lasalvia-Prisco

1. Applicant's response filed on 10/26/2006 is acknowledged. Claims 1-70 are pending. New claims 67-70 are added. Claims 1-64 and 66 are withdrawn from consideration as being drawn to non-elected inventions. Claims 60-63 and 65 are amended.

2. Newly submitted claims 68-70 directed to an invention that is independent or distinct from the invention originally claimed (i.e. claims 60-65) for the following reasons:

Claims 60-65 are drawn to a method of isolating blood plasma that comprises white blood cells. New claims 68-70 contain two extra steps, i.e. generating a plurality of tumor associated antigen-chaperone complexes in a plurality of malignant tumor cells in the patient, and causing the release of at least some of the plurality of tumor associated antigen-chaperon complexes into the patient's bloodstream, and further isolate the blood plasma. Claims 68-70 are further limited wherein the generating plurality of tumor associated antigen-chaperon complexes in the plurality of malignant tumor cells in the patient comprises inducing protein synthesis in the plurality of malignant tumor cells of the patient via administering a pharmaceutical compound to the patient, the pharmaceutical compound comprises insulin. New claims 68-70 are distinct from claims 60-65 because they comprise distinct steps and utilize different products which demonstrate that each method has a different mode of operation. Each invention performs this function using a structurally and functionally divergent material. For

example, the pharmaceutical compound and insulin, which are recited in new claims 69-70, are not required for the method of claims 60-65. For these reasons claims 60-65 and new claims 68-70 are patentably distinct. Furthermore, the distinct steps and products require separate and distinct searches. The inventions of new claims 68-70 encompass material that is claimed in terms of the plurality of tumor associated antigen-chaperon complexes, a pharmaceutical compound, insulin which are not required for the search of claims 60-65. As such, it would be burdensome to search the new claims 68-70 and claims 60-65 together.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 68-70 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 60-65 and new claim 67 are under examination.

4. The information disclosure statement (IDS) filed on 8/14/06 has been considered. A signed copy is attached hereto.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

6. The rejection of claims 60 and 65 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the term "fractioning" in claims 60 and 65 is withdrawn in view of applicants' amendment to the claims.

7. The rejection of claims 60-65 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the term "a blood specimen solution" in claim 60 is withdrawn in view of applicants' amendment to the claims.

Response to Arguments

8. The rejection of claims 60-65 and new claim 67 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the term "a supernatant plasma-cell layer", "plasma-cell solution" and "plasma-cell fraction" in claims 60, and 62–65 is maintained.

The response states that the recitation of a "supernatant plasma-cell layer" in independent claim 60 has been amended to recite a "supernatant of blood plasma comprising white blood cells," as disclosed in the specification on page 30, lines 11 and 12 and on page 47, lines 23-24 (see response page 26, 2nd paragraph, lines 1-5). The response states that "supernatant" as recited in the original claims is a "liquid or fluid forming a layer on the surface of another liquid", not an underlying intermediate or interface layer, as is incorrectly suggested in the office action (see response page 26, 2nd paragraph, lines 11-13). The response states that the "plasma-cell solution" is formed by inducing a hypotonic shock in the "supernatant of blood plasma" via dilution.

Applicants' arguments have been carefully considered but are not found persuasive. The amendment to the claims cannot overcome the instant rejection. The amended claims 60, 62, 63 and new claims 67 recite "a supernatant of blood plasma comprising white blood cells", and "supernatant of blood plasma". As defined by the specification, a blood specimen solution is a blood specimen extracted from the patient and added to an anticoagulant, such as heparin (see response page 26, lines 6-8). The conventional meaning of plasma is a supernatant of a blood specimen solution obtained after the blood specimen solution is settled for a period of time or is centrifuged. If the plasma is collected after the blood specimen solution is centrifuged, the plasma normally would contain few white blood cells because the white blood cells stay in the interface (buffy coat). If the plasma is collected after the blood specimen solution is settled for a period of time, the plasma would contain some white blood cells. Here, the claims recite the term "supernatant of blood plasma". The meaning of the term is unclear. What is the supernatant of plasma? Do applicants mean supernatant of a blood specimen solution? Furthermore, claims 60-65 and 67 are indefinite for reciting the term "plasma-cell fraction". The meaning of the term is unclear. It is unclear how the fraction is formed by just heating the plasma-cell solution?

Because of these reasons, the rejection is deemed proper and therefore maintained.

9. The rejection of claims 60-65 and new claim 67 under 35 U.S.C. 103(a) as being unpatentable over Lasalvia et al. (31st annual meeting of the ASCO, May, 1995, A730)

in view of Moingeon et al. (Vaccine 2001 (Jan), 19: 1305-1326), Ryan (US Patent No. 4,436,821, 5/13/1984), Freshney (Freshney, Culture of Animal Cells, A Manual of Basic Technique, 4th Edition, 2000, pages 423-424), Somani (US Patent No. 3,906,107, 9/16/1975), Colaco (US 2005/0175635 A1, effective filing date at least 2/22/2001), Moore (US Patent No. 5,328,844, 7/12/1994), Mejza (US Patent No. 6,416,992 B1, effective filing date at least 10/13/1999), Heldebrant (US Patent No. 4,490,361, 12/25/1984) is maintained.

The response states that the rejection is moot because the rejection is based on the incorrect assumption that the "supernatant," "plasma cell layer," and "plasma-cell solution" comprise plasma and an interface cell layer (buffy coat) and that the "blood specimen solution" consists solely of a blood sample (see response page 29, paragraph A). The response states that none of the cited references, either alone or in any combination, teach any autologous hemoderivative composition for use in eliciting an effective antitumoral immune response in a patient, much less, a method for the preparation of such a composition as recited in claims 60-65, either as originally filed or as amended herein (see response page 30, 4th paragraph). The response states that Moingeon does not teach an autologous hemoderivative composition, and further Moingeon teaches away from autologous compositions (see response page 31, 1st paragraph). The response states that none of other references teach the preparation of an autologous hemoderivative composition (see response page 31, 1st paragraph). The response states that Moore teaches lysing tumor cells with equal volume of distilled water, however, Moore does not teach or suggest the innovative autologous

hemoderivative composition of the present invention, further Moore teaches away from the instant invention because Moore teaches that autologous tumor cell vaccine are limited by the availability of surgical tumor specimen (see response page 33). The response further states that Heldebrant suggests heat as a means to sterilize, i.e. inactivate infectious agents including viral components which may be present in biological material such as a protein fraction separated from blood plasma. The use of heat in applicant's invention, however, is not for purpose of sterilization, rather, heat is utilized in the present invention to release tumor associated antigens (see response page 34, 1st and 2nd paragraphs). The response states that in the Declaration of Applicant, Dr. Lasalvia-Priso presents an independent review and analysis of the innovate method presented herein by way of the Commentary of Dr. Emens, a person with considerable expertise in the art (see response, page 35, 4th paragraph). Dr. Emens indicates that the novel and unique method of the present invention fulfills a long felt need in the art (see response, page 36, 1st paragraph). The Declaration of Dr. Garcia-Giralt has shown that following treatment with the inventive method disclosed herein, the patient appears to be in complete and total remission (see Declaration paragraph 13), and the complete and total remission of patient X is "completely unexpected" (see response page 36, 2nd paragraph). The response states that evidence present herein establishes that not only is the method of the present invention novel and non-obvious, but that it fulfills a long felt need in the art, and that unexpected results have already been achieved through its implementation.

Applicants' arguments have been carefully considered but are not found persuasive. The Declarations are insufficient to overcome the instant inventions. As indicated in the previous office action (see page 4, 1st paragraph), because the indefinite nature of the claims, claims are interpreted that the "supernatant," "plasma cell layer," and "plasma-cell solution" comprise plasma and an interface cell layer (buffy coat) and that the "blood specimen solution" consists solely of a blood sample. Nevertheless, claims as currently amended recite plasma comprising white cells, the plasma isolated by the method of Ryan would meeting this claim limitation because in Ryan's reference, the plasma was isolated from a blood sample by mixing the blood with an anticoagulant and separating from red blood cells using method such as settling (see previous office action page 6, lines 1-4). The plasma isolated by Ryan would contain white blood cells. In contrary to applicants' assertion that none of the cited references, either alone or in any combination, teach any autologous hemoderivative composition, Lasalvia teaches a method of treating metastatic cancer using autologous blood fraction (autologous blood derivative) from cancer patients (see abstract), and moreover Moingeon teaches that serum contains human tumor antigens, and human tumor antigens have been used in the art as cancer vaccines (see page 1311, left column). While other references do not teach that hemoderivative composition is useful for cancer treatment, this rejection is a 103(a) rejection. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Moingeon

reference is used in the rejection to show that lysing cells (any cells not just tumor cells) with distilled water is a well known method in the art. Moingeon does not teach away from instant invention. Moingeon teaches that use of tumor cell vaccine is limited by the availability of surgical tumor specimens. In view of this teaching, one of ordinary skill in the art would have been motivated to develop hemoderivative composition because Lasalvia teaches a method of treating cancer using hemoderivative composition. Furthermore, unlike the tumor cell vaccine which is obtained through surgical procedure, the hemoderivative composition can be easily obtained by noninvasive procedure. Applicants argue that the use of heat in applicant's invention is not for purpose of sterilization, rather is for releasing tumor associated antigens. In response to this argument, MPEP states that rational different from applicant's is permissible (see MPEP 2144). The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. >See, e.g., In re Kahn, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). In response to applicants' argument that the method of the present invention fulfills a long felt need in the art as shown by Declaration of Dr. Lasalvia-Priso and resulted in unexpected results as shown by Declaration of Dr. Garcin-Giralt, the Declarations have been carefully considered but are insufficient to overcome the instant rejection. Using autologous blood derivative to treat cancer has been known in the art as shown by the teachings of Lasalvia. Using vaccines comprising tumor associated antigens to treat cancer has also been known

before the instant invention was made as shown by the teachings of Moingeon. Moingeon further teaches serum contains human tumor antigens. Regarding the unexpected results, Lasalvia teaches that the total number of metastasis diagnosed in the autologous blood fraction treated group was statistically significant lower than that in the control group (see abstract). Lasalvia further teaches that more significant effect was seen in late metastases (see abstract). MPEP (MPEP 716.02) states that any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Because prior art has recognized the anti-metastases effect of the blood derived fraction, the instant invention does not provide the unexpected results. Furthermore, the instant claims are drawn to a method of isolating the blood plasma comprising white blood cell, because the method of collecting the blood plasma comprising white blood cells has been known in the art before the instant invention was made, and the combined references teach all the active steps of the methods, the blood plasma prepared according to the teaching of the references would have the same property as the one isolated by the method of claims 60-65. Finally, because the plasma or serum of a cancer patient contains tumor antigens, the teachings of the combined reference apply to the new claim 67. Because of these reasons, the rejection is indeed proper and therefore, is maintained.

Conclusion

10. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Dec. 15, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER